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* * * * * * * * * * * * * * * * * * * *

=> s peritoneal dialysis
          2516 PERITONEAL
          9145 DIALYSIS
L1         389 PERITONEAL DIALYSIS
                (PERITONEAL(W)DIALYSIS)

=> s peptide#
L2       12021 PEPTIDE#

=> s glucose
L3       28288 GLUCOSE

=> s l3 or des^Hxtrose
          11593 DEXTROSE
L4        35216 L3 OR DEXTROSE

=> s l2(P)l4
L5          526 L2(P)L4

=> s l5(L)l1
L6            7 L5(L)L1

=> d ti,^H^H^H^H^Hset high off
SET COMMAND COMPLETED

=> s lk^H1
          2516 PERITONEAL
          9145 DIALYSIS
L7         389 PERITONEAL DIALYSIS
                (PERITONEAL(W)DIALYSIS)


     (FILE 'USPAT' ENTERED AT 17:43:29 ON 12 APR 93)
L1         389 S PERITONEAL DIALYSIS
L2       12021 S PEPTIDE#
L3       28288 S GLUCOSE
L4       35216 S L3 OR DEXTROSE
L5         526 S L2(P)L4
L6           7 S L5(L)L1
                SET HIGH OFF
L7         389 S L1
                SET HIGH ON

=> s l7(L)l5
L8            7 L7(L)L5

=> d ti,pat,kwic 1-7

                                                    L8: 1 of 7
US PAT NO:      5,158,538 [IMAGE AVAILABLE]
TITLE:           Regulating peritoneal lymphatic drainage and uses
therefor
1.       5,158,538       Oct. 27, 1992      604/28          [IMAGE
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5,039,609 ✓

5,011,826 ✓

4,959,175 ✓

4,579,085

AVAILABLE]

DETDESC: DETD(68) As those skilled in the art will readily appreciate, if and when the particles themselves contain, or are associated with **glucose**, the **glucose** will contribute to the dialysis. Similarly, if and when the particles themselves are osmotically active or biodegrade or dissolve to. . . agents will also contribute to dialysis. Also, if and when the particles themselves contain, or are associated with, amino acids, **peptides**, or proteins, such can contribute to the nutritional status of the patient. Further, if and when the particles themselves contain,.

. .

US PAT NO: 5,092,838 [IMAGE AVAILABLE] L8: 2 of 7
TITLE: Histidine buffered peritoneal dialysis solution
2. 5,092,838 Mar. 3, 1992 604/27 [IMAGE AVAILABLE]

SUMMARY:

BSUM(13)

European Patent application No. 277,868 discloses the use of a glycine based **peptide** for stabilizing bicarbonate solutions for dialysis. The **peptide** disclosed also acts as an osmotic agent and therefore as an alternative to **glucose**.

US PAT NO: 5,039,609 [IMAGE AVAILABLE] L8: 3 of 7
TITLE: Osmotic agents for peritoneal dialysis
3. 5,039,609 Aug. 13, 1991 435/68.1 [IMAGE AVAILABLE]

SUMMARY: BSUM(12) The . . . the method for peritoneal dialysis which employs an osmotic agent which is not only a safe and beneficial alternative to **glucose**, but which also is economically feasible. It has now been unexpectedly discovered that a mixture of relatively low molecular weight. . . agent in a peritoneal dialysis solution; in comparison with an amino acid solution, the somewhat higher molecular weight of the **peptides** prevents the rapid uptake into the blood, allowing a more effective maintenance of the osmotic gradient as well as preventing the unwanted increase of nitrogen in the blood. The **peptide** mixture, which is ultimately, although very slowly, absorbed into the serum further provides a valuable dietary supplement, being derived from high-quality protein. Finally, the present **peptide** mixture provides an inexpensive and easily obtainable source of osmotic agent. Other **peptide** mixtures, used for medicinal purposes, have been previously described. For example, U.S. Pat. No. 4,427,658 describes a protein hydrolysate derived. . . protein. In that case, nearly total enzymatic hydrolysis was claimed to be performed, with no separation of larger from smaller **peptides**. Therefore, the resulting product apparently contains **peptides** of much larger sizes,

possibly up to 5000 daltons or more, in the final mixture. These may pose antigenic and/or. . .

DETDESC: DETD(22) In . . . based on the simple but unexpected combination of dialysis and reverse osmosis, has proven to be particularly amenable to the **peptide** separation required for the present product. However, its use is not limited to **peptides**; it may, in fact, be used for separation of virtually any type of low molecular weight solutes as, for example, starch or **glucose** as indicated hereinbefore. By "low molecular weight", as used in the present specification and claims, is meant molecules of about. . .

DETDESC: DETD(30) As noted above, the present method is particularly well suited to the preparation of mixtures of low molecular weight **peptide** mixtures and may be used commercially in connection with hydrolysis of other types of proteins, such as soybean, egg or milk proteins. It may also be readily applied to use with any other heterogeneous, non-**peptide** mixture from which it is necessary or desirable to isolate low molecular weight species as, for example, it may be. . . food processing industry as baking additives or sweeteners. If the enzyme activity is allowed to continue, the end product is **glucose**. The use of the present process allows the continuous isolation of maltodextrins of low molecular weight from an enzyme reactor,. . .

DETDESC: DETD(31) With respect to the present product, the purified **peptide** mixture can be combined with any osmotically balanced aqueous solution appropriate for use as a peritoneal dialysate. Useful dialysate must. . . contents of a typical dialysate solution is presented in Table 2, without the amount of osmotic agent specified; in a **glucose** solution, **glucose** monohydrate would typically be added in an amount from about 1.5-4.25%. It will be understood that this represents just one. . . a possible solution and that variations in the pattern will be apparent to the skilled artisan. The proportion of the **peptide** mixture in the dialysate can vary, but normally comprises in the range of about 1 to 15% by weight of dialysate solution. In any event, the amount of **peptide** used should be sufficient to confer, with supporting electrolytes an osmolality of about 300 to about 500 mOsm/l (280 mOsm/l. . . DETDESC:

DETD(46) The above components provide an osmolality of about 260 mOsm/l. To the above mixture is added 61.1 grams of the **peptide** mixture per water which provides an osmolality of approximately 126 mOsm/l, giving the solution as a whole an osmolality approximately equivalent to that of a 2.5% **glucose** solution.

DETDESC: DETD(48) Utilizing the **peptide** mixture of Example 1B in a solution as described in Example 3, experiments were carried out to compare the effectiveness of the low molecular weight **peptides** as osmotic agents relative to the

effectiveness of **glucose**.

DETDESC: DETD(49) The . . . in an A-B sequence, so that each rabbit served as its own control. Each animal was dialyzed with either 2.5% **glucose**, or alternately, with sufficient **peptide** to bring the osmolality of the solution to approximately that of the 2.5% **glucose** solution (385 mOsm/l). Each animal's peritoneal cavity was loaded to approximately 50 ml of dialysate per kg of body weight.. . .

DETDESC:

DETD(50)

Glucose Solution **Peptide** Solution

Vol. ml. Vol. ml. Gain Vol. ml. Vol. ml. Gain

Animal

t = 0 t. . .

DETDESC:

DETD(51)

At the same osmolality as **glucose**, the **peptides** show a nearly 100% increase in osmotic pumping activity at 60 minutes, apparently due to the lower rate of loss of **peptide** compared to **glucose** in the circulation. FIGS. 3 and 4 show plots of the average amine-end-group concentrations vs. time and the **glucose** vs. time in the peritoneum. These verify that only 20% of the **peptide** (measured by end groups) is lost, compared with nearly 35% of the **glucose** being lost. These results are even more significant in view of the fact that the **glucose** had not yet equilibrated to plasma levels at 60 minutes.

US PAT NO: 5,011,826 [IMAGE AVAILABLE] L8: 4 of 7
TITLE: Aqueous dialysis and rinsing solution for intraperitoneal administration

4. 5,011,826 Apr. 30, 1991 514/23 [IMAGE AVAILABLE]

SUMMARY: BSUM(13) At . . . a secondary role in peritoneal dialysis solutions, in particular because due to their unphysiological character (except for amino acids and **peptides**) negative long-term effects are observed which are due mainly to the metabolization after absorption being too low or too slow. To be mentioned here are hyperosmolar plasma states when using the sugar alcohol sorbite and xylite, cumulation of **glucose** polymers and glycerin, allergic reactions with gelatin and toxicity of synthetic polymers. Substances with higher molecular weight (hydroxyethyl starch, dextrans,. . . other substances is still to be found. In addition, technical

problems are encountered in the sterilization of amino acids or **peptides** together with reducing sugars as calorie carriers by formation of toxic substances (Maillard reaction).

SUMMARY: BSUM(28) If as further optional osmotically active substance the dialysis solution according to the invention contains **glucose** in addition to galactose, the quantity ratio is advantageously 1:3 to 3:1, preferably 1:1. The dialysis solution may however if desired contain not only **glucose** but also for example fructose, sorbite, xylite, glycerin, modified gelatins, carbohydrates, amino acids and/or **peptides** as further optional osmotically active substance(s).

L8: 5 of 7

US PAT NO: 4,959,175 [IMAGE AVAILABLE]
TITLE: Solution for dialyses and use of peptides based on glycine for preparing it

5. 4,959,175 Sep. 25, 1990 252/364 [IMAGE AVAILABLE]

SUMMARY: BSUM(19) Apart from the **peptide** based on glycine, the solution of the present invention contains all the constituents customarily used for the preparation of a solution for dialyses; these constituents can be chosen, in particular, from sodium, chloride, potassium, calcium and magnesium ions and **glucose** and/or mixtures thereof; but other constituents may be used, such as sulfate or citrate ions. The pH and the stability . . . invention depend, as is quite obvious, on the respective amounts of its various constituents, and especially on the amount of **peptide** based on glycine which is incorporated.

SUMMARY: BSUM(20) In addition, this **peptide** has also proved to play the part of an osmotic agent, and the amount of it in the solution of the present invention is accordingly inversely proportional to that of an osmotic agent such as **glucose**.

DETDESC: DETD(49) With the object of assessing the ultrafiltration capacity of the dialysate containing bicarbonate and **peptides** based on glycine, a direct perfusion of 40 ml/kg of the dialysate d- (1.5% of **glucose**, 415 mosmol/kg) is performed into the peritoneal cavity of rabbits.

L8: 6 of 7

US PAT NO: 4,906,616 have this already
TITLE: Hydrolyzed sodium casein compositions for dialysis procedures

6. 4,906,616 Mar. 6, 1990 514/21

DETDESC:

DETD(4)

The use of **peptides** to provide the osmotic gradient in dialysis has inherent advantages over the sugar-based solutions used hitherto. The molecular size of the bulk of the **peptides** (about molecular weight 1100 and greater) ensures that diffusion

across the peritoneal membrane will be minimal. This has four important consequences. First, the osmolality of the **peptide** solution will be maintained for a much longer period than with **glucose** and amino acid solutions since both **glucose** and amino acids diffuse very rapidly across the membrane with concomitant reduction in the osmotic effectiveness of the solution in the peritoneum. for this reason the **peptide** solution will exert a greater osmotic effect over a longer period of time and hence require less frequent replacement of the dialysis fluid with a corresponding reduction in the risk of infection. Second, the absence of **glucose** removes a complicating factor in the treatment of diabetic patients and in the long term treatment of all patients. Third, any leakage of small **peptides** into the patient's bloodstream will present no metabolic problems and, indeed, may provide a small but useful supplement to the nitrogen content of the patient's diet. Fourth, the **glucose**-based solutions previously proposed have to be adjusted to pH for 5.3 to 5.5 or thereabouts to prevent degradation of the **glucose** during heatsterilisation: since the **peptide**-based solution of the present invention does not suffer from this disadvantage, it may be used at normal physiological pH value.

. .

L8: 7 of 7

US PAT NO: 4,574,085
TITLE: Method for using dialysis solution containing glycerol

7. 4,574,085 Mar. 4, 1986 424/680

SUMMARY: BSUM(20) The . . . patients, particularly pediatric patients on chronic peritoneal dialysis, suffer serious protein loss due to the diffusion of amino acids and (poly)**peptides** from the blood into the peritoneal dialysis solution. Accordingly, by this invention, such protein loss can be counterbalanced, and a. . . of an amino acid source material in the peritoneal dialysis solution in accordance with this invention. Such a solution, when **glucose**-free, may be readily sterilized because of the compatability between glycerol and amino acids at sterilizing temperatures.

SUMMARY: BSUM(30) Glycerol is rapidly metabolized in the body, with a greatly reduced need for insulin when compared with **dextrose**, so that the peritoneal dialysis solution of this invention is particularly advantageous for use with diabetics. Also, the ultrafiltration rates. . . to provide a protein nutrient to the patient during the peritoneal dialysis process by diffusion of the amino acids or (poly)**peptides** into the bloodstream.